VANDERPOEL (W.B.)

Albuminuria without Manifest Organic Renal Lesion

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WALDRON B. VANDERPOEL, M.D.

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ALBUMINURIA WITHOUT MANIFEST ORGANIC RENAL LESION.[1]

THE topic I propose to present for your consideration will appeal strongly to that individual for whose benefit so much medical literature has of late years been written, the general practitioner, as on his correct diagnosis and proper treatment will here, in an unusual degree, depend whether the patient will enjoy many years of full or comparative health or the reverse; to the examiner for life insurance it presents one of his most difficult problems, and on his clear reading of the case will depend large financial interests as well as his professional reputation, and the popular estimate of the exactness of medical science.

Clinicians have long been familiar with a class of cases in which the only abnormal symptom has been the passage, constantly, or from time to time, of small or even large amounts of albumin in the urine, and this extending over a period of months or years. To these cases have been applied the names of functional, physiological, paroxysmal, intermittent, cyclic, or chronic albuminuria by different writers, according to the standpoint from which they viewed them.

To Dr. Bright, of England, we owe our first clear idea of the clinical importance of albuminuria, as portrayed in his "Reports of Medical Cases," 1827 and 1831, and the subsequent elaboration of the same is largely due to the investigations of Christison, Rayer, Frerichs, Traube, and

[1] Read before the New York Academy of Medicine, Section in General Medicine, October 17, 1893.

others. For a long time it was considered sufficient to ascertain the presence of proteid matter to pronounce the case a renal affection, in all probability a nephritis, and the worst prognosis was accordingly drawn. It is now well known that we may find in the urine several other proteid bodies besides albumin, each bearing its own significance, and the presence of many depending on causes widely remote from the kidneys. In point of time we find that Sir Robert Christison,[1] in 1839, pointed out that certain articles of diet sometimes caused a temporary albuminuria. Jaccoud,[2] in 1864, laid down the proposition that there are cases of persistent albuminuria in persons in otherwise good health. Moxon,[3] in 1878, published a paper on "Chronic Intermittent Albuminuria." Professor George Johnson,[4] of England, in 1879, announced his observations on the occurrence of albumin in the urine of persons otherwise apparently healthy. Later we have many writers, notably Pavy,[5] who designated these cases as "cyclic" or "physiological;" Grainger Stewart, Sir William Roberts, Professor Fraser, Mahomed, Finlayson, Saundby, Tyson, Pye-Smith, Goodhart, Ralfe, and others in England; Senator, Jaksch, Virchow, and others in Germany; Capitan, Chateaubourg, C. Finot, Dieulafoy, and others in France; Millard, W. H. Porter, Munn, Washburn, W. B. Davis, Da Costa, and others in our own country.

The opinions held as to the frequency of the occurrence of albuminuria in otherwise healthy persons differ widely. Some, notably Posner[6] and Senator,[7] claim that

[1] Granular Degeneration of Kidneys, 1839.

[2] Nouv Dict. de Méd., vol i., Paris, 1864. Quoted in the British and Foreign Medico-Chirurgical Review, April, 1868, and by G. Stewart, Lectures on Albuminuria.

[3] Guy's Hospital Reports, vol xxiii.

[4] British Medical Journal, 1879, vol ii. Latent albuminuria.

[5] Lancet, vol. ii., 1882; British Medical Journal, 1883, vol. i.; New York Medical Journal, July 16, 1892.

[6] Virchow's Archiv, lxxix.

[7] Albuminuria in Health and Disease. New Sydenham Society, 1884.

their observations warrant the belief that repeated examinations, over long periods and at different hours of the day, will eventually show albumin in every healthy person, and that we may regard an albuminuria as physiological, just as we recognize a physiological glycosuria, oxaluria, or indicanuria. Washburn[1] reports he has confirmed these results with picric acid and other delicate tests in fifty persons, finding albumin in all. Sir William Roberts[1] says that concentrated urines from persons of undoubted health are comparatively rarely free from traces of albumin detectable by direct testing. In ordinary processes of testing these traces are naturally overlooked, but certainly exist very frequently, and their existence shows how nearly on the verge of a sensible albuminuria healthy persons are. Others report varying percentages, viz.: Chateaubourg,[2] 592 in 701 persons examined = 84 per cent.; Capitan,[3] 44 in 98 soldiers = 44.9 per cent.; Van Noorden, 3 to 35 per cent. in German soldiers under differing conditions of rest or fatigue; Grainger Stewart,[4] 31 per cent. in 407 examined, and therefrom formulates the statement that it will be found in one in three of the male population if examined during the active period of the forenoon, an hour or two after breakfast; before breakfast the proportion would be considerably smaller; Edes, 10 to 20 per cent.; Munn,[5] 24 in 220 examined = 10.9 per cent.; Washburn, of Milwaukee, 5.91 per cent. in 338 examined; Shepherd, 2 per cent. in 35,471 examined. These differences are difficult to reconcile; they may, in part, be due to varying conditions of seasons, pursuits, and habits of the subjects examined, also thoroughness of the observers, etc.; still we may have to conclude that they have given more attention to this subject and been more systematic in their examinations in foreign countries.

[1] Medical News, Philadelphia, 1893, vol. i., p. 341; vol. ii., p. 119.
[2] Medical Chronicle, 1884. Urinary and Renal Diseases, 4th ed. G. Stewart. Lecture on Albuminuria.
[3] Annual Univ. Medical Sciences, 1893.
[4] Lectures on Albuminuria.
[5] MEDICAL RECORD, vol. xv.

In considering the subject of albuminuria, we must recognize two primary forms, viz., one whose origin is entirely extrinsic or remote from the kidneys, often called false albuminuria, and the other, intrinsic or true, depending on changes in the renal circulation or structure; but followed in their later history it becomes difficult, if not impossible, to draw any sharp dividing line in these cases, as those which at first were purely extrinsic by their persistency and secondary effects, frequently become true or intrinsic, and a knowledge of their prime nature only to be attained from a study of the chemical nature of the proteid bodies presented in the urine.

Clinically, we may group these albuminurias under a threefold heading, under which may be brought all the varied cases reported by different writers, viz.: I. Simple albuminuria without preceding or accompanying symptoms, persistent or intermittent, and giving no indication from urinalysis of organic renal lesion. II. Uric acid or oxaluric form. III. Neurotic form.

I. **Simple Albuminuria**.—To this class can be assigned all those cases which continue for years without any apparent deviation from the normal in health, presenting no preceding or accompanying symptoms of disturbance in the digestive, circulatory, or nervous functions, and would never have been discovered except accidentally, either in the routine examination of the urine by the family physician or by the insurance examiner on the subject's application for a policy in life insurance. These are the true functional or chronic albuminurias.

As causes we find prominent: 1, dietetic; 2, exposure to cold or cold bathing; 3, muscular activity; 4, mental strain or worry, prolonged brain activity.

1. *Dietetic.*—(*a.*) The mere ingestion of food markedly favors the appearance of albuminuria where the predisposition already exists. Grainger Stewart reports, as to the effect of the taking of food, that he examined the urine of 32 soldiers before breakfast and after, finding

albumin in 5 in the former and in 13 in the latter, and in a total of 160 examinations of soldiers, old men, and children, in twenty per cent. before breakfast, thirty-five per cent. after. Ch. Finot[1] reports albumin in 5.5 per cent. before breakfast, and in 11.6 per cent. at midday.

Capitan and Chateaubourg confirm these results. Pavy states that albumin is frequently absent from the early morning urine and appears later in the day after the first meal has been taken, and then gradually falls off in amount to a mere trace at bed-time. His habit is to require four specimens of urine for examinations, one at the rising hour, one at noon, one at 6 P.M., and one at bed-time.

(*b.*) Some persons manifest an idiosyncrasy toward certain articles of food, developing albuminuria after their ingestion. These are especially eggs, cheese, buckwheat cakes, pastry, meat, etc. The peculiarity is most marked where the amounts consumed are large. Stokvis[2] reports experiments in animals with egg-albumin, introduced by the stomach, rectum, and subcutaneously, resulting invariably in the appearance of egg-albumin in the urine. Injection of serum-albumin in an animal of the same species was negative, unless the quantity was sufficient to raise the blood-pressure considerably. The results from ingestion into the stomach of human beings have not been so uniform, some experimenters, as Drs. Lauder Brunton,[3] Dobradin, and Maguire failed to produce albuminuria by swallowing a number of raw eggs in rapid succession, while D'Arcy Power and Claude Bernard succeeded in so causing it. Grainger Stewart details a series of experiments from which he reaches the conclusion that, in general, the introduction of raw egg albumin into the stomach induces albuminuria, always in

[1] La Semaine Médicale, February 17, 1892.

[2] Recherches expérimentales sur les conditions pathogénique de l'albuminurie, 1867.

[3] Pharmacology, Therapeutics, and Materia Medica, p. 435.

small amount, and it is not egg-albumin but serum-albumin; also that all albumin disappears from the urine when ordinary diet is resumed. The same results have been obtained in experiments with cheese and the other articles mentioned.

The explanations offered for these conditions are conflicting, and not in all cases clear. The form following the mere ingestion of food may at times be due to an already impaired or diseased gastric or intestinal function, resulting in an imperfect metabolism and the development of toxic products in the blood which cause direct renal irritation in their excretion, or again, under certain conditions, the renal circulation may be influenced, either reflexly through the nervous system, or directly by a plethoric condition of the blood, so as to allow of a transudation of albumin. In the form depending on idiosyncrasy toward albuminous foods, it was formerly held that egg-albumin was directly absorbed into the blood and discharged as such from the kidneys, this being rendered more plausible by arguments showing that the molecules of this form of albumin were smaller, hence more transfusible. Five explanations are now entertained by different writers: *a*. That there is a condition of overcharge of the blood with albumin and some of the excess escapes in the urine. *b*. That severe digestive disturbance is produced and uric acidæmia or oxaluria developed, bringing these cases under our second main classification. *c*. In accordance with the theory of Dr. Thomas Oliver,[1] of New Castle, that urea is mainly formed from the red blood-corpuscles, and most when the liver is at its highest activity during digestion, considering that the liver would very likely be unusually stimulated by the excessive amounts of nitrogenous matters presented to it, and hence the blood-corpuscles destroyed in larger numbers, we would have a corresponding excess of albumin liberated, and this not being at once transformed into urea, appears in its own form in the urine. Credit is due to

[1] British Medical Journal, November 27, 1886.

Drs. Rolfe[1] and Noël Paton[2] for investigations upon which this theory is based. *d.* Animals in whom albuminuria had been artificially produced by the ingestion of large amounts of albuminous substances by Semmola, were killed, and the lesions of well developed glomerulo nephritis were invariably found in their kidneys, undoubtedly due to the irritant effects of the egg-albumin. Hence we have in this case an actual organic lesion. Millard claims this to be true in a large percentage of these cases, and cites as proof a case reported by Christison, which eventually died of Bright's disease; also a patient reported by Germain Sée had all the symptoms of Bright's disease; and Claude Bernard, whose experiments we have quoted, himself died of Bright's disease, apparently. *e.* Increase of the salts of the blood, and also of urea; the latter we may expect after a meal such as we are considering, favor osmosis, and hence may induce exudation of albumin.

2. *Exposure to Cold or Cold Bathing.*—The existence of a form of albuminuria due to this cause was first described by Dr. George Johnson, of England, in 1879. Grainger Stewart gives as results from an examination of 21 boys, on rising, albumin in 4; after cold plunge bath, 5. There was an increase also in the amount of albumin in each. As causes we have mainly reflex nervous action on the renal circulation from peripheral irritation, and also increased excretory work thrown on the kidneys by the suspension of the perspiratory function of the skin.

Dr. Sewill describes a patient now living in his seventy-seventh year, who, twenty-six years ago, was markedly albuminuric. The causation was later assigned to undue indulgence in sea-bathing in cold weather. Family history good, and he had always been healthy. He was fleshy, indolent, and a large flesh eater, took alcohol in moderate amount. In the course of four or five illnesses during the past twenty years, albumin had been found, but his health was not seriously impaired, although he dis-

[1] Diseases of Kidneys, 1885. London Lancet, 1886, vol. ii.
[2] Journal of Anatomy and Physiology, January, 1886.

regarded all dietetic regulations. Three years ago an ascites and abdominal abscess appeared, and his life was despaired of. He is now well and hearty, and scoffs at regimen, etc. Dr. Sewill cites this case as showing the difficulty presented to insurance examiners in determining proper risks.[1]

3. *Muscular Activity.*—We are made familiar with this cause for albuminuria by the observations of Grainger Stewart, of the urine of foot-ball players and soldiers after a long march. Weston, after his long walk in London, had both albumin and casts in his urine. Under the same category fall all states, conditions, or pursuits which involve any tax on the physical powers; thus we have cases occurring among blowers of wind instruments, after parturition, and finally a form depending wholly on posture. Pavy[2] instances a young collegian aged eighteen, a good athlete, who stood a civil service examination, but albumin being found in his urine, he was rejected. The case was cyclic, however, and he was afterward passed. He went to Oxford, and from there went up for a final physical examination before going out to India. Having meanwhile read up the literature of these cyclic cases, he remained in bed until just prior to his examination and was accepted, there being a temporary cessation of the albuminuria. The erect posture evidently acts in these cases as violent exercise does in the more robust. There exist wide differences in the reports of different observers. Chateaubourg gives 201 cases in 230 soldiers examined. Griswold,[3] in 24 examinations after three- to four mile walks and other vigorous exercise followed by cold baths, failed to find any albumin. Van Noorden reports 23 cases out of fifty-three samples of soldiers' urine after exercise, viz., forty three per cent. Millard[4] explains these differences as due to faults in testing, and claims that all the conditions of muscular fatigue, riding, marching, etc.,

[1] Annual Universal Medical Sciences. 1893. [2] Ibid.
[3] Philadelphia Medical News, June, 1884.
[4] Bright's Disease, Third Edition. New York: William Wood & Co.

favor an increase of secretion of mucus from the lower urinary passages, and especially if there should exist slight irritation of the urethra, prostate, or bladder, the remains of an old gleet or cystitis. To differentiate between albumin and mucin is very difficult and requires very delicate and carefully applied tests, together with the systematic use of the microscope, by which accompanying conditions characteristic of mucinuria may be discovered. Under this heading appropriately fall cases attending upon manifestations of chorea and epilepsy, considered from a view of the muscular activity accompanying them, although they are usually classed under the neurotic type and their causation considered as due entirely to nervous phenomena.

The kind of albumin found in this class of cases by different investigators has varied; Dr. Maguire reports a varying amount of paraglobulin, and draws a prognostic inference that, the greater its amount in proportion to that of serum albumin, the more favorable the case; Pavy finds alkali albumin sometimes instead of serum albumin. Dr. Oliver,[1] of Harrogate, reports a case of intermittent albuminuria in which peptones replaced albumin for a long time. Again, Grainger Stewart tells us sugar may replace or accompany albumin, and he deduces from this proof of the theory that faulty metabolism has also here much to do with the production of the condition. Other chemical changes mentioned by Stewart are excess of phosphates in addition to, or alternating with, albumin; urates may be very abundant and sometimes uric acid, but most common of all, oxalate of lime.

The explanation of these cases offered by Stewart is altered blood-pressure in the Malpighian tufts and renal blood vessels; he claims as confirming this the metabolic abnormalities just mentioned, as indicating like influences in the hepatic circulation, possibly. It has been found that increased arterial pressure does not favor albuminuria, but increased venous pressure and slowing of

[1] Bedside Urine Testing. Third Edition.

circulation do materially favor it; hence many of the mechanical cases, viz., pressure of abdominal tumors and the gravid uterus on the renal veins or ureters. Operating in like manner on the renal circulation was a case recently reported of intussusception[1] of the right ureter; also a case due to a retroverted[2] uterus, where correction of the faulty uterine position resulted in disappearance of the albumin.

The strain to which the kidneys are subject in eliminating the excess of excrementitious products resulting from muscular activity, forms another potent factor.

4. *Mental Strain or Worry, Prolonged Brain Activity, etc.*—Fürbringer records the case of a medical man who showed albumin only as a result of mental excitement, all the ordinary excitants of this condition failing to produce it. Altered blood-pressure in the renal vessels depending on direct nervous influence from the brain, will explain the origin of these cases. Here may be classed all cases due solely to reflex nervous influences, and as such we may possibly view the case of retroverted uterus just cited, if its effect can be considered due to pressure on nerve trunks.

II. **Uric Acid or Oxaluric Form.**—The characteristics of this class have been clearly portrayed by Da Costa.[3] As the name indicates, the distinguishing feature is the appearance in the urine of an excess of uric acid crystals or urates, amorphous or crystalline, or crystals of calcium oxalate. The actual quantity of urine passed remains normal, but the amount of solids is increased, and it is often spoken of as loaded or concentrated urine, specific gravity 1.022 to 1.028, or 1.036. Chlorides are normal or increased in amount, never diminished, as they are uniformly with contracted kidney. Phosphates and urea normal or increased. Casts, hyaline or epithelial, may

[1] London Lancet, March 8, 1890. See quoted in Annual Medical Sciences, 1891, G. 15.

[2] New York Medical Journal, June 22, 1893.

[3] American Journal of the Medical Sciences, January, 1893.

or may not be present. Albumin usually small in amount and may vary with the time of day, being most in the early urine and possibly absent in the evening. In our testing we must again be careful to avoid error from mucin, which is liable to be abundant in these urines. The clinical significance of each ingredient varies, but they all indicate a defect in the assimilative functions, and especially so do uric acid and the urates, which in some cases are due to imperfect oxidation into urea, but for the most part trace their origin to imperfect hepatic functioning. This condition is predisposed to by (1) over-indulgence in a not sufficiently mixed diet, either nitrogenous or carbonaceous. In moderation carbonaceous food is easy of transformation, but in excess the hepatic function is overtaxed and its powers impaired for acting on the more arduous nitrogenous substances. Excess in nitrogenous diet will manifestly prove a still greater tax. (2) A possibly inherited condition called the uric acid oxlithemic diathesis. This is a sensitive or vulnerable condition of the liver and kidneys, in which they are more prone than ordinary to suspend their functions. This state many writers, notably W. H. Porter,[1] consider due to generations of abuse of those organs, and not correctly a diathesis. Regulation of diet will largely, if not entirely, cause its disappearance. Oxalate of lime bears the same clinical import; some vegetables contain an abundance of this substance, and may favor in their consumption an oxaluric condition, as do also nervous worry and strain.

The cause of albuminuria here is probably a purely mechanical one, depending on the irritation produced by the imperfectly formed metabolic products, and markedly so by the sharp crystals of lime oxalate or of uric acid. These crystals may lodge in the renal tubules by accretion, attain a moderate size, and cause a persistent albuminuria following after an intermittent one. Altered blood pressure in the kidneys may be produced reflexly through irri-

[1] Renal Disease. William Wood & Co., 1887.

tation of the pneumogastric branches in their final distribution, and so contribute another cause; and again chemical changes may occur in the blood as still another cause.

No marked symptoms may attend these cases which would indicate any disturbance of the digestive, circulatory, or nervous functions, and they may continue for years undiscovered and never result in any organic kidney disease. More commonly we get a clear history of prolonged irregularities of diet followed by functional digestive disorders, manifested by uncertain appetite, flatulence, etc., and later nervous symptoms, viz , headache, sleeplessness, vertigo, etc.; and circulatory disturbances, viz., irregular pulse, usually feeble, but may exceptionally show increased tension and some rigidity.

A symptom to which Da Costa draws marked attention is a slight rise in temperature, particularly in the afternoon, which he interprets as signifying increased renal activity, due to the excess of imperfectly formed excrementitious substances they are called upon to eliminate.

Under this category a number of the so-called dietetic albuminurias, primarily in part, and eventually wholly, fall, that is, where we have secondary digestive disturbances inaugurated and a true mal-assimilative albuminuria developed. Da Costa ranks here also the majority of the cases of this affection in boys, called by most writers the albuminuria of adolescence. Sir William Gull[1] speaks of this adolescent form as occurring in boys and young men about as often as spermatorrhœa.

Many writers consider they can trace in this class of cases the uric acid type, a true pre-Brightic stage, so called, which, if allowed to continue untreated, will eventually develop the rigid arteries, persistent high tension pulse, and retinal changes of chronic nephritis, and contracted kidney. An interesting paper detailing cases illustrative

[1] London Lancet, 1886, vol. i.

of this condition, and tracing the sequence of events, was read by Dr. R. Van Santvoord[1] before the New York Academy of Medecine a short time ago, in which he shows that it is not unusual, where dyspeptic symptoms have continued more or less constantly over a long period of months or years, for organic changes to appear, manifested lastly in the circulatory system by continued high pulse-rate and tension indicative of commencing arterial sclerosis and cardiac hypertrophy, the cause possibly being ptomaïnes or other toxic substances, derived from defective metabolism, circulating in the blood.

III. **Neurotic Type.**—We have here cases following or accompanying manifestations of epilepsy, chorea, apoplexy, hysteria, influenza, exophthalmic goitre, and Stewart reports a case accompanying infantile paralysis, also one with multiple sclerosis, and again with the general paralysis of the insane. Puncture[2] of the floor of the fourth ventricle, near the location which causes glycosuria, Bernard showed some time ago, would produce albuminuria, and we have like effect from lesion of the cerebral peduncles, also from section or irritation of the spinal cord.

The explanation of these cases generally accepted is direct nervous influences acting from the brain or spinal cord through the splanchnic, cœliac, and renal nerve plexuses, by whose irritation the vessels of the kidneys are contracted and by their paralysis dilated; in the latter case the volume of the circulation, not the rate, is increased, and secretion correspondingly increased.

There remain a few forms of albuminuria which I have been unable to assign to any class enumerated, as their etiology is to me obscure; such are a form mentioned by Dr. Lambert[3] as attending extremes of temperature, an-

[1] Arterio-renal Disease, MEDICAL RECORD, January 14, 1893. p. 36. Read before the Section on General Medicine, December 20, 1892.

[2] Pepper's System of Medicine.

[3] Medical Director of Equitable Life Insurance Company, quoted by W. B. Davis. Albuminuria in the Apparently Healthy.

other found largely in the newly born, and lastly, after anæsthesia in some cases.

Let us consider the prominent clinical features presented, and endeavor to ascertain the value and bearing of each upon our diagnosis, prognosis, and treatment. This is of unusual importance here, as a diagnosis can often be made only by exclusion, hence the import of each symptom must be carefully weighed.

1. *Pulse rate and Tension.*—In the simple non-organic forms the pulse is normal in rate and usually feeble. While these conditions remain the case may be considered purely functional and such have been accepted by insurance companies and proved good risks. When the pulse-rate and extension are both constantly increased, we may justly consider that we have to deal with a commencing cardiac hypertrophy and arterial sclerosis, and our prognosis will be grave if the condition is at all well advanced.

2. *Albumin.*—A study of the amounts or persistency of this substance affords little light, since in advanced forms of nephritis it may be constantly absent or appear only at times, and is uniformly scanty. Again, the quantity may be large and constant, and the subsequent history prove the case wholly functional. Jaksch[1] warns us that we are not warranted in inferring the existence of a renal lesion from the mere fact that the urine contains albumin. The forms of albumin usually found and always alluded to as of pathological interest, are serum albumin and serum globulin or paraglobulin; these two occur in all albuminous urines in varying proportions, the latter frequently the most abundant.

With these may be associated other and adventitious forms from which they may with difficulty be distinguished. Many find their way into the urine after its secretion, being derived from disintegration of the renal epithelium or due to the presence of blood, pus, prostatic or seminal fluid, leucorrhœa, etc.

[1] Clinical Diagnosis, 2d English edition, translated by Cagney.

Grainger Stewart classifies these albumins as follows: Hæmoglobin, peptone from gastric or intestinal digestion, propeptone, albumoses or globuloses, acid albumin derived from the action of acids on albumin, alkali albumin, fibrin found in hæmaturia, chyluria, and also derived from renal casts, mucin, lardacein, waxy or amyloid material derived from renal casts occasionally. The microscope and clinical history will usually differentiate serum albumin and globulin from these adventitious forms with ease, except mucin, which affords a fruitful source of error as it forms a precipitate with most all the test reagents, and its appearance is favored by the same causes as albumin. Sir William Roberts says it is present in all urines, healthy or morbid. W. H. Washburn regards its appearance as suspicious, and where persistent in large amount it affords strong proof of defect in the renal structures, and may be diagnostically as important as the albumin which it masks. Citric acid is the usual and most delicate test, and should always be used when testing for albumin to determine the presence and proportion of mucin, since this acid does not precipitate albumin. Dilute mineral acids behave the same, but concentrated ones dissolve mucin. Millard mentions as a possible source of confusion the sticky substance found in chronic cystitis, attributed to the decomposition of leucocytes by the urea and ammonium carbonate; the microscope will here prove of service.

The tests for albumin have, of late, greatly multiplied, but coagulation by heat, the oldest, and the nitric acid or Heller's test, next in age, still rank first with the majority of examiners. Grainger Stewart considers picric acid the most delicate and reliable test, whose first use in England he attributed to Dr. George Johnson.[1] From experiments with different urines he shows that this acid gives a more marked and rapid precipitate with albumin than with mucin, which with experience can be easily distinguished, and in many cases minute quantities of al-

[1] London Lancet, 1882, vol. ii., p. 737.

bumin may be detected without any precipitate from mucin, even though abundant. Millard recommends the phenic-acetic acid and potash test:

B. Acid phenic glacial	ʒ ij.
Merck's or Calvert's 95 per cent. acid acetic puri	ʒ vij.
Add. liq. potassæ	℥ ij., ʒ vj.

Tanret's test, or the double iodide of mercury and potassium, is considered of value by the same author. The nitric-magnesian test discovered by C. Gerhardt[1] in 1856, and modified by Sir William Roberts,[2] consists of one part nitric acid to five parts saturated solution of magnesia sulphate, claimed to be more delicate than pure nitric acid. Other tests are metaphosphoric acid, acidulated brine, potassium ferrocyanide, ammonium sulphate, etc. The percentages claimed for each test are: heat, 1 part in 100,000; nitric acid, 1 to 100,000; Tanret's phenic-acetic acid and potash, and nitric magnesian test, 1 to 200,000. For the accurate determination of the amount of albumin present we have several elaborate methods of separation: drying and weighing, also Esbach's tubes graduated for the urine and reagent, Sir William Roberts's dilution method, and Dr. Oliver's percentage method. Millard says the percentage is usually less than one-tenth per cent., and the most he ever found less than two and one half per cent., an amount he considers never exceeded. He criticises the frequent method of guessing at the amount from the degree of cloudiness, and the statement often made of three and four and even fifty per cent., while the serum of blood contains only three to four per cent., and urine with one and one-half per cent. would become almost solid in testing, and look one-half albumin. Hofmann and Ullzmann offer an approximate, but fairly accurate, method in considering every line of thickness of the white cloud caused by contact with the reagent, to represent one-tenth per cent. of albumin.

[1] Traité de Chimie organique. [2] Medical Chronicle, 1884.

In considering the relative values of the different tests, Dr. Victor C. Vaughn [1] states that the only tests which distinguish the albumins from the albumoses and peptones are heat, nitric acid, and acetic acid, and potassium ferrocyanide; Sir William Roberts recommends heat or nitric acid contact; Professor Fraser, Tyson, Pye-Smith, Goodhart all favor the same. A few precautions are necessary in applying the heat test, viz., to render the urine moderately acid, if not so, but not too acid, or we will get an acid albumin not precipitable by heat; acetic acid is preferred for this purpose. Earthy phosphates, if abundant, may give a cloud which should be cleared up with an acid—citric, nitric, or acetic, preferably the latter; but care is required, as when the cloud from albumin is faint the addition of anything will scatter it, and nitric acid will redissolve such a trace.

With the nitric acid test the acid is usually added slowly, drop by drop, but recent writers recommend placing the acid in the tube first, and pouring the urine gently upon it. Urates in excess may obscure this test, and when so they may be dissolved by heating the test-tube to a point just below the coagulating point of albumin, viz, 140° F. Dr. Munn [2] and others call attention to the fact that this and all contact tests should be viewed by reflected light; the tube should be held at the lower end of the window, the shade drawn down to it and out from the window about a foot, thus excluding the direct light from the eye of the observer; the acid is added while the tube is thus held. Dr. Munn claims that by this precaution many cases will be detected which would otherwise be overlooked, and that he has thus succeeded where the family physician of the applicant for life insurance had failed. He also cautions that the tested urine should stand for five minutes, Millard says ten or fifteen, before deciding, and then if no cloudiness appears the urine is non-albuminous.

[1] W. B. Davis: Albuminuria in the Apparently Healthy.
[2] MEDICAL RECORD, vol. xv.

In concluding this topic I quote from Rudolf von Jaksch,[1] "Serum albumin in notable quantities is never found in healthy urine, and its appearance is in all cases a morbid symptom of great importance."

3. *Urea.*—In this substance we have an exponent of the working capacity of the kidneys. Persistent diminution in the daily excretion of the urea would point clearly to existing or impending organic renal disease. The amount is influenced by the quantity of fluid consumed, kind of food, amount of exercise, and condition of digestive functions. Average daily output should be 550 grains (W. H. Porter).[2] Excretion is diminished by the onset of acute febrile diseases, later increased, and all causes which retard the activity of the hepatic or renal cells, especially the latter, and most markedly by organic renal lesions. Hence in the functional forms of albuminuria the excretion of urea should remain normal. The source of urea is from the destruction of the red blood corpuscles (Dr. Oliver), and from the food ingested, from nitrogenous most directly, from carbonaceous by a more complex process.

4. *Casts.* The origin of these bodies is in the renal tubules, from an albuminous or fibrinous exudate from the blood-vessels, and they usually incorporate the tubular epithelium in their structure. They are found in most all forms of renal congestion and inflammation in varying amounts, but as to what exact conditions favor their formation, and why at times present and again absent under the same apparent physical conditions, we are unable at present to determine. Usually their discovery is of grave diagnostic and prognostic import, but hyaline, epithelial, and even granular casts have been found in cases which eventually completely recovered and may at the time have appeared in perfect health in all other respects. Charcot[3] states that hyaline casts may be found

[1] Clinical Diagnosis. 2d English edition, translated by Cagney.
[2] Renal Diseases. William Wood & Co. 1887.
[3] Bright's Disease, p. 33.

in normal urine, and many other observers have found them in affections apparently apart from the kidneys; *e.g.*, Nothnagel says he always found them in severe icterus, albumin is frequently found here also; Grainger Stewart reports casts as frequently found in such cases. Allchin does not consider casts as a serious symptom. A cause for error in reports may possibly be mucous casts or cylindroids which have the shape and many of the appearances of hyaline casts, or may receive a precipitate of amorphous urates or lime phosphate, and closely simulate granular casts. Sir Andrew Clark,[1] Dr. Campbell Black, and others report bodies resembling renal casts which were really prostatic casts. Again, Drs. George Johnson and Millard deny that casts or renal epithelium are ever found in normal urine. In my private records I have notes of a case which occurred in a gentleman forty years of age, of fine physique, fond of athletic exercises, especially boxing. Hyaline casts were repeatedly found by the examiners of two prominent insurance companies in this city, and these results confirmed by Drs. Delafield and Janeway. His application for a policy was rejected. Subsequent investigation disclosed that the casts were only present after boxing and absent at all other times. An accessory fact on which much stress has been laid, was, that he invariably followed his exercise with a cold alcohol and water sponge-bath. As to the bearing of exercise on this phenomenon we may cite Weston again, as after his long walk in London, one hundred and fifteen miles in twenty-four consecutive hours, he is reported by Pavy to have had in his urine albumin and casts, hyaline and granular, but twelve hours later all was normal. The case I have related was unique in that albumin was not present at any time. Change in his habits of exercise resulted in disappearance of casts. Six months later he was accepted by both companies, and to day, nine years later, is in perfect health and vigor, fully justifying his acceptance as an in-

[1] London Lancet, 1886, vol. i.

surable risk. Casts have never since been found in repeated examinations. What explanation can be offered for the condition here narrated? Exercise might, where violent, increase the excretory products to be eliminated and so subject the kidneys to a strain sufficient to cause a congestion, and even low grade of inflammation, and so produce casts; but if so why did not albumin accompany? Again, the cold alcohol sponge-bath might affect the renal vaso-motor nerves reflexly through peripheral irritation. This patient was at times markedly oxaluric, and shortly before the casts were discovered, six or nine months, he had a slight urethral discharge, apparently prostatic, which I attributed to oxaluria; now, the same irritation in the kidneys might cause cast formation, possibly.

5. *Specific Gravity.*—If this is high we may safely assume that the kidneys are functionating properly, particularly if the daily quantity is normal; but if the specific gravity remains permanently low, grave organic renal disease is probable.

6. *The Daily Quantity.*—This affords an indication of the filtration activity of the kidneys. The amount is large in waxy or cirrhotic kidney. It is small in obstructive troubles in the urinary tract, also in degenerative conditions of the renal epithelium and in chronic congestion. In functional albuminuria the amount should be about normal, and influenced simply by usual causes, viz., atmospheric temperature and moisture, and by diet. A fair daily output would be 40 to 50 ounces.

As a cause of increased urinary secretion, Porter[1] mentions loss of contractility in the renal vessels, and the full blood pressure, unrestrained by the afferent vessels, being brought to bear on the Malpighian tufts, is forced through the over strained capillaries.

7. *Color.*—This varies from pale or almost colorless, in nervous or diabetic cases, to dark or even black. These grades of shade may depend on the concentration of the

[1] Renal Diseases, p. 205.

urine, and so be of importance to our topic as indicating what the daily quantity should be, or are due to certain articles of diet, certain drugs, or to abnormal products from the patient's own economy, as bile, or blood.

8. *Phosphates, Urates, Chlorides, Oxalates.*—These have already been considered.

9. *The General Personal Appearance.*—This may give some clew to the renal condition in a peculiar pallor, possibly some disinclination to exercise, poor circulation, and transient œdemas of the feet or eyelids, although the appearances with organic lesions resemble these but are more intense.

To sum up, we find as causes of albuminuria: 1. Changes in the renal circulation, viz., venous stasis, the venous radicles and Malpighian tufts being dilated, tension therein increased and circulation slowed; or again, all the renal vessels dilated, arterial, capillary, and venous, with increased rapidity of circulation, that is, an active or passive hyperæmia. In no purely non-organic albuminuria do we have increased arterial tension, except transitory or accidental; if persistent, arterio-sclerosis is developing and the case has become an incipient nephritis. These changes in the renal circulation may depend upon cardiac or obstructive pulmonary affections, tumors of the mediastinum or abdomen, causing pressure on the vena cava or other vessels, or lastly, on change in the renal structure. 2. Changes in the renal blood-vessels in all their coats which permit the transudation of albumin, while under normal conditions this would be impossible. 3. Digestive disturbances which produce irritating substances for the kidneys to excrete. 4. Changes in the blood; *a*, surcharge of albumin; *b*, an excess of salts which, Hoppe-Seyler and others consider, favor the exosmosis of albumin; *c*, increased wateriness claimed by some as a factor, viz., Magendie and Mosler;[1] *d*, the opposite condition, undue concentration, is maintained by others, G. Stewart, etc. 5. Reflex or direct nervous

[1] G. Stewart: Lecture on Albuminuria.

influences. 6. Small amounts may be derived from a slightly excessive disintegration of renal epithelium without any pathological import (Senator). 7. Lastly, the adventitious, contingent, or accidental forms from parts remote from the kidneys.

Prognosis.—We find here much difference of opinion. The factors demanding our attention in arriving at a satisfactory and logical conclusion are the duration, persistency, and amount of the albumin, together with the other characteristics of the urine, and the general physical condition and pursuits of the subject.

Dr. George Johnson says, "If albumin is absent during intervals of twenty-four hours consecutively, urine normal in color and specific gravity and no casts, prognosis is good."

Professor Saundby: "He has seen a large number of such cases during the past ten years who have never developed Bright's disease, and many are well."

Pavy: "Where traces of albumin only without other conditions of kidney disease, and especially where present at one part of the twenty-four hours and not others, prognosis good."

Drs. Maguire and Broadbent[1] consider albumin only of importance in a relative manner, as indicating other lesions present.

M. Dieulafoy[2] reports that in sixty renal cases in his hospital wards albumin was absent in one-fourth, and in others albumin disappeared and yet the disease progressed.

Grainger Stewart[3] cites the case of a young man whom he watched through his student career, in the arduous work of a four years' course in medicine, who had albumin constantly in his urine, and yet the work he went through should be sufficient guarantee that his health was not seriously impaired.

Dr. Barnes[4] expresses the view "that the condition in-

[1] London Lancet, 1893, vol. i., p. 999.
[2] Ibid., p. 1542.
[3] Lectures on Albuminuria.
[4] London Lancet, March 18, 1893.

dicates a temporary disturbance of the equilibrium of several functions, and the incapacity of certain organs has to be supplemented by the activity of others, and if neglected the condition may become pathological."

Dr. Ralfe,[1] in an able paper read before the London Medical Society, says: "The clinical significance of albuminuria as a symptom has undoubtedly diminished during the last twenty years. By the systematic examination of the urine in all patients presenting in private practice and for life insurance, these cases are discovered earlier and treatment instituted before irreparable damage has been done. Hence, the prognosis is improved." A large number of these cases, he says, eventuate in the red or white granular contracted kidney. In the former, the onset being insidious, the case rarely comes under observation until well advanced, but when seen early much benefit may be obtained by diet and proper hygiene. He cites the case of a gentleman now living, seen first in 1878, for bronchitis, then presenting no abnormal urinary or other symptoms. In 1882, he had hypertrophy of left ventricle and displacement of apex. Pulse showed increased tension; urine, abundant; specific gravity, 1.014, a trace of albumin. Under diet, etc., albumin disappeared, and now, after eleven years, he has a little more outward displacement of apex, a more palpable thickening of the radial vessels, and more constant appearance of albumin and of urine of low specific gravity. So far no serious symptoms have developed, but how long before they may we cannot say. Cases with the small, white, or mottled kidney give more marked symptoms, are seen earlier, and hence offer a better prog nosis.

The gouty form, our uric or oxaluric form, Dr. Ralfe gives a favorable prognosis for if under proper diet, etc.; but neglected, the results are often disastrous. The history of a case is given which terminated fatally in four years through neglect of diet, etc.

[1] London Lancet, February 25 and April 8, 1893.

Albuminuria occurring for the first time in adult life, Dr. Ralfe considers a danger signal, even though no cardiac hypertrophy, etc., accompany and the albuminuria be intermittent.

Dr. W. T. Gaerdner,[1] of Glasgow, expresses much the same view and says that the danger signal is not necessarily fatal, but heeded, may avert disaster. Dukes[2] gives an unfavorable prognosis in all cases at all persistent.

Brannan[3] pronounces that all cases untreated will eventuate in organic renal lesion.

Dr. Pye-Smith[4] considers all albuminurias pathological.

Millard the same. Dr. W. H. Washburn[5] says he considers the condition always pathological and indicates an abnormal state of the kidneys, which may be transitory or permanent, the probability of cure diminishing as it lasts. My own views, based upon cases encountered in private practice, dispensary, and hospital work, also cases examined for life insurance or referred to my care by insurance examiners, have led me to regard these cases with distrust, especially where the cause appears to reside in any persistent fault in the assimilative functions, nervous or circulatory apparatus, and only to relax those feelings when the albumin has disappeared for weeks or months, and the other characteristics of the urine become entirely normal. Undoubtedly, many cases show albumin in the urine persistently for years and never develop any further indications of organic disease, but the natural tendency in even the blandest cases, is to gradually impair the renal epithelium and other structures by the continued abnormal filtration of albumin, and transform a simple functional into a true nephritis. Hence I would pronounce them damaged lives to be carefully watched, our diagnosis to

[1] London Lancet, March 11, 1893.
[2] Ibid., 1891, vol. ii., p. 1383.
[3] British Medical Journal, 1891, vol. ii., p. 136.
[4] Ibid., August, 1889.
[5] Philadelphia Medical News, 1893, vol. i., p. 341; vol. ii., p. 119.

be guarded, and if insured, only in a protected manner. As to insurance, Sir William Roberts and Senator consider these cases as favorable if purely functional. Pavy says, "I do not consider medical knowledge is at present in a position to enable us to differentiate these cases from those which eventually develop into Bright's disease."

Johnson favors an advanced premium. Saundby, assurance for five years and then re-examination. Pollack[1] holds the same view and an advanced premium.

It has been suggested to insure these cases at ordinary premiums, and if they die before the average first-class life limit, to deduct proportionately from the amount paid; but should they attain to the above limit or over, to allow full premiums.[2]

Treatment.—This is mainly dietetic, and regulation of the general hygiene, viz., occupation, clothing, exercise, etc. Diet plain, farinaceous or milk, few meats, and no wines. Keep the kidneys well flushed, using plain or alkaline mineral waters, hot water before meals. Warm bathing and free stimulation of the perspiratory glands. Repeated urinalyses to keep us informed of the working condition of the kidneys, and a watchful care of the heart and blood-vessels. As to drugs, most all observers have reached the conclusion that they are powerless to check the discharge of albumin, although several will produce it. An occasional hepatic stimulant, as blue pill or nitro-hydrochloric acid, will be of service. By these means a case may long be held in abeyance, and possibly even an entire cure effected.

Case I.—B. L——, merchant, aged forty-five. Family history and habits good. Rejected by insurance company in 1880 because albumin was found in his urine. Height, five feet ten inches; weight, one hundred and eighty pounds. Chest examination, negative. Digestion at times impaired, acid eructations, uncertain appetite; albumin scanty, but uniform. Ordered to travel,

[1] Medical Handbook of Life Assurance.
[2] Tyson, of Folkestone: London Lancet, March, 1893.

light diet, and regular hours for meals. Six months later improved, but still albumin found. Seen three months later, no albumin and general health good.

Case II.—L. McA——, aged twenty three; seamstress, unmarried. Seen first, in 1881, in hospital. Suffers from dysmenorrhœa, poor circulation, cold extremities, migraine, and attacks of hystero epilepsy. Heart sounds feeble, pulse weak and intermittent. Urine loaded with oxalate of lime and considerable albumin. Treatment: Calomel in grains iij doses, occasionally. Nitro-hydrochloric acid, and tr. nux vom., bromides for nervous condition. Diet: Milk, farinaceous articles, light meats, and fish. The urine improved with her general condition, but albumin never all disappeared. Discharged after three months, improved. Seen two years later, had remained benefited, but still had a trace of albumin, and showed some hypertrophy of left ventricle. Readmitted to hospital in 1887, suffering from uræmic dyspnœa, rigid and tortuous arteries, marked retinal changes, œdema of limbs, urine contains urates in abundance, albumin, casts fatty and granular. Died two weeks later in uræmic coma. Autopsy revealed small red kidney and general arterio sclerosis.

Case III.—J. W——, horse raiser, aged thirty seven. Seen first in 1884, suffering from albumin in the urine, but scanty; backache, nausea, frontal headache. Heart and lungs all right. Treatment: Diuretics, regulation of bowels, and later tonics; and in six weeks all abnormal symptoms, both general and in urine, removed. Seen during the next four years at intervals, remains free from albumin, and in good health. In 1892 seen, after an interval; has been passing albumin for six months, has granular and epithelial casts, headache, rigid arteries, apex displaced outside nipple line, accentuated aortic second sound. Treatment: Diuretics and stimulation of skin and bowels. Improved, but went West in cold weather, and returned much worse, and died of pulmonary œdema two weeks later. This was at the last a

case of contracted kidney, but originally was of the functional variety.

CASE IV.—Girard L——, seen in 1882 while participating in a walking match. aged twenty two, formerly telegraph operator, well developed, general physique good. Suffering from great prostration on third day of walk. Urine shows albumin, urates, and phosphate in excess. Ordered to discontinue walk, and all albumin disappeared.

CASE V.—Sam P——, longshoreman, seen in 1883. After a severe day's work in the sun in July, was prostrated and taken home in dazed condition; urine albuminous for two days.

CASE VI.—George C——, aged sixteen, delicate lad, seen in 1886 during an attack of chorea of great severity; urine albuminous. Chorea improved under Fowler's sol., large doses, and albumin disappeared at same time.

CASE VII.—C. K——, painter, aged fifty-two, suffering from bad colic. When seen in 1889 general condition fair. Urine albuminous for three weeks while under treatment, and then disappeared permanently.

CASES VIII., IX., X., XI., all in good general health, but at times show albumin in urine after irregularities in meals, hours, or excess in drinking; have been under observation now, 1, 3, $3\frac{1}{2}$, and 5 years, respectively. General health good.

CASE XII.—I. S. L——, Chinese art student, aged twenty-two, seen in 1884 suffering from incipient phthisis. Some pulmonary consolidation; urine has albumin and hyaline casts. Under tonics and travel his phthisis was checked, and with it the urine became normal and remains so now.

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